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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LONG, SCOTT	
ART UNIT	**PAPER NUMBER**
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/685,693	WEST ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42,45-69,71-83 and 85-158* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26,33,34,60-69, 71-77,80,89,90,92,94-102 and 158* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 27-32,35-42,45-59,78,79,81-83,85-88,91,93 and 103-157.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed 16 July 2007.

Election/Restrictions

The Examiner acknowledges the Remarks regarding the withdrawal of claims not directed to elected species. According to the examiner's understand of 37 CFR 1.142(b), cited below, it is appropriate to withdrawn claims drawn to unelected species. Furthermore, the original Restriction Election (11/20/ 2006) was elected without traverse and was made final in the First Action (1/11/2007).

37 CFR 1.142. Requirement for restriction.

(a) If two or more independent and distinct inventions are claimed in a single application, the examiner in an Office action will require the applicant in the reply to that action to elect an invention to which the claims will be restricted, this official action being called a requirement for restriction (also known as a requirement for division). Such requirement will normally be made before any action on the merits; however, it may be made at any time before final action.

(b) **Claims to the invention or inventions not elected, if not canceled, are nevertheless withdrawn from further consideration by the examiner by the election**, subject however to reinstatement in the event the requirement for restriction is withdrawn or overruled.

The examiner further quotes from the previous Action (filed 1/11/2007):

Examiner acknowledges the election, with traverse, of Group I (claims 1-102) directed to *ex vivo* methods of identifying genes and determining relative timing of transcriptional activation or repression of said genes in stem cells during differentiation, in the reply filed on 20 November 2006. The examiner also acknowledges the election, without traverse, of Species Ia, a nucleotide sequence that encodes a protein, specifically a fluorescent protein, which read

on claims 1-14, 16-80, 83-90, 92, and 94-102. The examiner also acknowledges the election, with traverse, of Species I-5, a human embryonic stem cell, which read on claims 1-42, 60-83, and 89-102.

Because no argument for the traversal was provided by applicant, thus the traversal is non-persuasive and the restriction is made final.

Because the applicant elected a variety of species within Group I, as required by the examiner's request for Restriction/Election, the examiner believes he is correct in withdrawing the unelected claims. The examiner hopes that the discussion above clarifies for the applicant the actions taken in regard to this issue.

Claim Status

Claims 1-4, 6-9, 11, 14, 15-18, 20, 22, 25-26, 33-34, 36-38, 42, 45, 47, 57, 59-64, 65-67, 69, 71, 73-81, 85-99 are amended. Claims 43-44, 70, and 84 are canceled. Claim 158 is newly added. Claims 27-32, 35-59, 78-79, 81-88, 91-93 and 103-157 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-26, 33-34, 60-69, 71-77, 80, 89-90, 94-102 and 158 are under current examination and will be examined to the extent to which they read on *ex vivo* methods and the species elections cited above.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 22 August 2007 consisting of 1 sheet(s) are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit from provisional U.S. Application No. 60/418,333, filed 16 October 2002. The instant application has been granted the benefit date, 16 October 2002, from the application 60/418,333.

Response to Arguments - Claim Objections

Applicant's arguments, see page 30 and Claim amendments, filed 16 July 2007, with respect to claims 16, 67 and 70 have been fully considered and are persuasive. The objections to claims 16, 67 and 70, have been made moot by the claim amendments submitted on 16 July 2007 and are hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – 35 USC 112, second paragraph

Applicant's arguments, see pages 30-31 and Claim amendments, filed 16 July 2007, with respect to claims 1-17 and 64 have been fully considered and are persuasive. The rejections of Claims 1-17 and 64 under 35 USC 112, second paragraph, have been made moot by the claim amendments submitted on 16 July 2007 and are hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 102

Applicant's arguments (Remarks, pages 31-32) and claim amendments filed 16 July 2007 have been fully considered and they are found persuasive.

The applicant argues that Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998: pp 4622-4631) do not teach or anticipate claims 1-8, 16-26, 60-69, 71, 90, 94-96, as amended. Particularly, the applicant points out that the method described by Stanford et al. does not teach the application of their method for determining relative timing of transcriptional activation in human stem cells. The examiner agrees with the applicant that the method of Stanford et al. is directed to determining relative timing of transcriptional activation in mouse stem cells.

Therefore, the examiner hereby withdraws the rejection of claims 1-8, 16-26, 60-69, 71, 90, 94-96 as anticipated by Stanford et al. under 35 USC 102(b).

Response to Arguments - Claim Rejections 35 USC § 103

Applicant's arguments (Remarks, pages 32-39) and claim amendments filed 16 July 2007 have been fully considered and they are found partially persuasive.

Stanford in view of Nehls:

Claims 1-8, 10, 16-26, 60-76, 90, 92, 94-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998: pp 4622-4631) in view of Nehls et al (US Patent 6,218,123, issued April 17, 2001). Applicant's arguments (Remarks, pages 32-35) and claim amendments filed 16 July 2007 have been fully considered but they are found unpersuasive. Therefore, the claims remain rejected for the reasons of record and the comments below.

The applicant offers three particular arguments to overcome the rejection of the instant claims: (1) the claim amendments have made the rejection moot, (2) each of the references do not teach all of the limitations of the instant claims, and (3) there is no motivation to combine the references and/or the examiner used impermissible hindsight reasoning in combining the references.

In regard to argument 1, directed to limitations of the newly amended claims not being taught by the combination of Stanford and Nehls, the examiner disagrees with the applicant. While Stanford does not teach a gene trap method which uses human embryonic stem cells, Nehls teaches, "gene trap selection is employed...[on]...preferred target cells include...embryonic stem cells, and particularly human embryonic or other

stem cells" (column 4, lines 40-43). This particular limitation, directed to applying gene trap methods to human embryonic stem cells is taught by one of the references, particularly Nehls et al.

In regard to argument 2, directed to the applicant's arguments that each of the references does not all of the limitations of the newly amended claims, the examiner agrees with the applicant. Although, not explicitly framed in such a way, the applicant has argued the two references (Stanford et al. and Nehls et al.) separately. However, MPEP 2143.01 suggests that this strategy is insufficient to overcome the combination of references: "One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)."

In regard to argument 3, directed to the motivation to combine references, the examiner disagrees with the applicant. In the previous action, the examiner wrote, "The person of ordinary skill in the art would have been motivated to make those modifications because fluorescent proteins, such as Green Fluorescent Protein (GFP) are functionally equivalent to lacZ (β-galactosidase) systems and do not require further reagents, such as X-gal, for visualization, as is the case for β-galactosidase. In addition, Stanford et al. teach that gene trap analysis of human embryonic stem cell gene expression is important for "understanding normal physiological processes and human disease" (page 4622, column 1)." (Action, page 10, filed 1/11/2006). In addition to the motivation provided in the prior action, the examiner asserts, the examiner

suggests that in light of the recent KSR decision, this necessity for a "reason or suggestion" is no longer required. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision Ex parte Smith, --USPQ2d, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396). Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (a method for determining the relative timing of the transcriptional activation or repression of a gene in a human stem cell, comprising use of a gene trap system) are taught by Stanford et al. or Nehls et al. It would be therefore predictably obvious to use a combination of these elements in a method applied to human embryonic stem cells. The methods of combining the elements, for example, "GFP" are further known in the art and are predictable; therefore they are likewise obvious.

Therefore, the examiner hereby maintains the rejection of claims 1-8, 10, 16-26, 60-76, 90, 92, 94-100 under 35 USC 103 as obvious over Stanford et al. in view of Nehls et al.

Stanford1 in view of Stanford2:

Applicant's arguments (Remarks, pages 35-36) and claim amendments filed 16 July 2007 have been fully considered and they are found persuasive.

The applicant argues that Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998: pp 4622-4631) in view of Stanford et al (Nature. October 2001. Vol.2, pp. 756-768) do not teach all the limitations of claims 1-10, 16-26, 60-69, 71, 77, 80, 90, 94-96, and 101-102, as amended. Particularly, the applicant points out that the methods described by both Stanford et al. references do not teach the application of their methods for determining relative timing of transcriptional activation in human stem cells. The examiner agrees with the applicant that the methods of the Stanford et al. references are directed to determining relative timing of transcriptional activation in mouse stem cells.

Therefore, the examiner hereby withdraws the rejection of claims 1-10, 16-26, 60-69, 71, 77, 80, 90, 94-96, and 101-102 as obvious over Stanford et al. in view of Stanford et al. under 35 USC 103.

Stanford1 and Stanford2 and Odorico:

Applicant's arguments (Remarks, pages 36-38) and claim amendments filed 16 July 2007 have been fully considered and they are found persuasive.

As described above, the Stanford references do not teach the application of their methods for determining relative timing of transcriptional activation in human stem cells. Because the Odorico et al. reference was added to the Stanford references to satisfy

limitations of claim 89 directed to forming a teratoma and the examiner did not specifically point out a rationale directed to applying the method to human stem cells, the examiner agrees with the suggestion of the applicant.

Therefore, the examiner hereby withdraws the rejection of claim 89 as obvious over Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998: pp 4622-4631) in view of Stanford et al (Nature. October 2001. Vol.2, pp. 756-768) as applied to claims 67, 71, and 77 above, and further in view of Odorico et al (STEM CELLS. 2001;19:193-204) under 35 USC 103.

Stanford1 in view of Chajut:

Applicant's arguments (Remarks, pages 38-29) and claim amendments filed 16 July 2007 have been fully considered and they are found persuasive.

As described above, the Stanford reference does not teach the application of their methods for determining relative timing of transcriptional activation in human stem cells. Because the Chajut et al. reference was added to the Stanford reference to satisfy limitations directed to forming a generating stage specific differentiation-specific genes in embryonic stem cells and the examiner did not specifically point out a rationale directed to applying the method to human stem cells, the examiner agrees with the suggestion of the applicant.

Therefore, the examiner hereby withdraws the rejection of claims 1-2, 11-14, 18, and 33-34 as obvious over Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998:

pp 4622-4631) in view of Chajut et al (WO/2002/086089, filed, April 23, 2002) under 35 USC 103.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26, 33-34, 60-69, 71-77, 80, 89-90, 94-102 and 158 are rejected under 35 USC 103(a) as obvious over Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998: pp 4622-4631) in view of Nehls et al (US Patent 6,218,123, issued April 17, 2001)

and further in view of Stanford et al (Nature. October 2001. Vol.2, pp. 756-768) and further in view of Odorico et al (STEM CELLS. 2001;19:193-204) and further in view of Chajut et al (WO/2002/086089, filed, April 23, 2002) and further in view of Prelle et al. (Anatomia, Histologia, Embryologia. June 2002; (31)3: 169-186) and further in view of Thomson et al. (Science Nov 1998; 282: 1145-1147).

The instant invention is directed to a method for determining the relative timing of the transcriptional activation or repression of a gene a human stem cell that occurs when the stem cell differentiates, wherein the stem cell is an inner mass cell, an embryonic stem cell, and embryonic germ cell, an embryoid body cell, a morula-derived cell, or a partially differentiated embryonic stem cell, comprising: (a) randomly inserting into the genomic DNA of a human stem cell in a population of stem cells a marker DNA construct comprising a nucleotide sequence that encodes a detectable product and is not operably linked to a promoter; (b) culturing the stem cell ex vivo under conditions in which the stem cell differentiates; (c) monitoring the differentiating stem cells to detect changes in the level of expression of the marker DNA construct in the cell; and (d) detecting a change in the level of expression of the marker DNA construct in the differentiating cell; and (e)correlating the change in the level of expression of the marker DNA construct with the differentiation of the cell, thereby determining the relative timing of the change in the level of expression of a gene in these cells.

Stanford et al. (Blood, Vol 92, No 12 (December 15), 1998: pp 4622-4631) (hereafter Stanford1) teach "random insertion of exogenous DNA into single sites in the mammalian genome" (page 4622, column 2). Stanford1 apply this method to identify

and characterize a large number of genes capable of lineage-specific expression in murine embryonic stem cells during differentiation (page 4622, column 2). The system uses a promoterless *lacZ* reporter gene that catalyzes a chromogenic product, when integrated downstream of an endogenous promoter (page 4623). The ES cells were grown for a series of days (page 4624, column 1) until the "transcriptional activation of the trapped gene" (page 4624, column 2) and subsequent *lacZ* expression (blue staining) during *ex vivo* differentiation (page 4624). Stanford1 teach, "pattern and levels of *lacZ* expression" (page 4626-4627) at various stages of differentiation of ES cells into hematopoietic and mesodermal lineages. Stanford1 teach differentiation of isolated clones of gene trapped ES cells (page 4628, figure 4). The method of Stanford1 further comprises sequence analysis of gene where integration occurs (page 4622, abstract). Stanford1 teach totipotent embryonic stem cell lines (page 4622, line 2). Stanford1 teach their method identifies multiple genes (page 4622). The method of Stanford1 further utilizes Southern Blotting and hybridization (page 4624, column 1). Stanford1 identified two or more different genes which are transcriptionally activated at different times during differentiation into a particular cell type (page 4625, table 3). Stanford1 assayed to detect a change in expression of LacZ polypeptide (page 4624). Stanford1 teach induction of stem cells to progenitor cells of hematopoietic and vascular cell lineages and further differentiation into fully differentiated "circulating blood cells" (page 4626, column 2). Stanford1 teach the further development of the ES cells into embryoid bodies (EB) (page 4624, Results). The teachings of Stanford1 include use of

RACE PCR to determine mRNA expression. Stanford1 also utilize RACE fragment probes for hybridization.

Stanford1 does not teach the use of human embryonic stems cells in their method, but does satisfy the limitation of some species of claim 4, particularly murine ES cells. Also, Stanford1do not teach the use of fluorescent proteins in their gene trap construct, but rather utilize the colorimetric catalyzing *lacZ* gene, which is one of the unelected species listed in claim 5. Stanford et al. does not explicitly teach a method that employs more than one marker gene within the same cell, but clearly teach the use of a single marker within multiple cells.

Nehls et al. teach methods of screening gene trap cassettes integrated into the genome comprising selectable markers, including chromogenic and fluorescent markers (column 4, lines 20-25). The "gene trap selection is employed...[on]...preferred target cells include...embryonic stem cells, and particularly human embryonic or other stem cells" (column 4, lines 40-43). Nehls et al. teach, "selectable marker may be expressed by control elements present in the vector, or, preferably, the selectable marker is only expressed under the control of an endogenous, i.e. cellular, promoter. This feature allows one to select for both the integration event, and also better insures that the construct has integrated within a cellular gene." (column 4, lines 25-31).

In particular, Nehls et al. teach a method of gene trapping employing multiple selectable markers (column 3, line 41) and multiple genes (Figure 4) expressed by endogenous promoters (column 4, line 28).

Nehls et al do not specifically teach changes in levels of expression, because of their invention utilizes a normalized library isolated from stem cells.

Stanford et al. (Nature. October 2001. Vol.2, pp. 756-768) (hereafter Stanford2) teach a method to "increase the versatility of trapping, several groups have modified vectors to include recombination sites,...permits additional modifications to be made to a trapped locus, such as co-opting the promoter elements of the trapped gene to drive the expression of a knocked-in transgene for use in...cell-labeling experiments" (page 763, column 1). The teachings of Stanford2 meet the further limitations of claim 101, requiring integration of DNA comprising recombinase gene and recombination sites and gene expressing detectable product. In particular, Stanford2 teach the limitations of claim 77, specifically "homologous recombination in embryonic stem (ES) cells" (page 759, column 2) and "random mutagenesis" (page 759, column 2).

Odorico et al. teach, "in vitro differentiation of ES cells transduced with gene trap vectors can be used to discover novel developmentally regulated genes that are important in tissue specific differentiation programs" (page 196, column 1). Odorico et al. further teach, "Human ES cells injected into severe combined immunodeficient mice form benign teratomas, with advanced differentiated tissue types representing all three EG layers" (page 197, column 2).

Neither Stanford reference teaches a method generating differentiation stage antibodies from purified cells or cell extracts.

Chajut et al. teach "present invention relates to the identification of genes involved in proliferation and differentiation of embryonic stem cells" (page 1, lines 11-

12). Chajut et al. teach, "present invention provides for use of said differentiation factor for determination of the differentiation stage of selected cells." (page 12, lines 4-5). Chajut et al. further teach, "antibodies may be prepared against the immunogen or antigenic portion thereof, for example,...the natural gene product and/or portions thereof" (page 19, Antibody production) and further describe immunization of non-human mammals to produce antibodies (page 20).

Chajut et al. does not teach methods of identifying genes using the gene trap system.

Prelle et al. teach, "The in vitro differentiation capacity of ES cells provides unique opportunities for experimental analysis of gene regulation and function during cell commitment and differentiation in early embryogenesis. Recently, pluripotent stem cells were established from human embryos (Thomson et al., 1998) and early fetuses (Shamblott et al., 1998), opening new scenarios both for research in human developmental biology and for medical applications, i.e. cell replacement strategies." (page 169, Summary).

Thomson et al. teach, "embryonic stem cell lines derived from human blastocysts" (page 1145, title) and in vitro differentiation of human embryonic stem cells. Thomson et al. further teach, "Screens based on the in vitro differentiation of human ES cells to specific lineages could identify gene targets for new drugs, gene that could be used for tissue regeneration therapies, and teratogenic or toxic compounds" (page 1146, middle and last paragraphs).

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to combine the teachings of Stanford1 in view of Nehls et al and further in view of Stanford2 and further in view of Odorico et al and further in view of Chajut et al. and further in view of Prelle et al. and further in view of Thomson et al. to apply a method for determining the differential expression of genes in human embryonic stem cells using a gene trap strategy.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the claimed elements are taught by Stanford1 or Nehls or Stanford2 or Odorico or Chajut et al. or Prelle et al. or Thomson. Specifically Stanford1 teaches all of the elements of claim 1, except its application to human stem cells. Prelle, in particular, indicates a motivation to study of gene regulation and differentiation in human embryonic stem cells and suggests that Thomson has developed methods of screening human embryonic stem cells which identify target genes specific to differentiation. Together with the basic teachings of Stanford and the other recited references, it would be therefore predictably obvious to use a combination of teachings to apply known methods to human embryonic stem cells.

Therefore the method as taught by Stanford1 in view of Nehls et al. and further in view of Stanford2 and further in view of Odorico et al. and further in view of Chajut et

al. and further in view of Prelle et al. and further in view of Thomson et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JLE